Docket No.: 0259-0411PUS1
**(PATENT)**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:
Maurizio Dalle CARBONARE et al.

Application No.: 10/019,387 | Confirmation No.: 6340

Filed: March 26, 2003 | Art Unit: 1612

For: USE OF HYALURONIC ACID DERIVATIVES FOR THE PREPARATION OF PHARMACEUTICAL COMPOSITIONS AND BIOMATERIALS FOR THE PREVENTION OF THE FORMATION AND URE OF CUTANEOUS SCARS | Examiner: S. Maewall

## ZANELLATO DECLARATION 2 - DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Anna Maria Zanellato, do hereby declare the following:

1. Attached is a copy of my *curriculum vitae*.

2. I am working as Scientific Assistant to the Patent Department at Fidia Farmaceutica and I have worked in the field of cellular biology for 13 years.

3. I am familiar with the above referenced patent application, as well as the development, usages and properties of hyaluronic acid derivatives and their uses, in particular to reducing normotrophic scarring.

4. I have read and understand the subject matter of the Office Action of September 04, 2008.

5. My prior Declaration executed on February 3, 2009 discussed experimental reports and offered comments in support of the patentability of the instant invention. That Declaration was submitted to the USPTO with an Amendment on February 3, 2009.

6. I offer the following comments in further explanation of the experimental results submitted with my prior Declaration, and to respond to some questions I understand were raised by the Examiners during an interview on February 25, 2009.

7. Explanation of the test result graph in Attachment 2 – I understand the Examiners questioned the meaning of the results in the graph of Attachment 2 of my prior Declaration, namely the graph of the results of the test for "Areas of scarring". I understand that the Examiners questioned why the areas of scarring for samples A and B are low at day 1, are then about equal to C and D on day 3, and then are again reduced at days 14 and 42.

7.1. The process of wound healing involves three major overlapping phases: lag phase (inflammation and cytokine release), proliferation phase (epithelial cells and fibroblasts migration and proliferation, connective tissue deposition and angiogenesis), and remodeling phase (with cell number decreases and collagen fiber organization). (See Exhibit 1)

7.2. During the initial healing phase encompassing the first three to four days after wounding, the process of wound healing is initiated by thrombogenic stimuli, and immune cells infiltrate the injury site where platelets release a variety of cytokines and growth factors. Therefore, during this phase, inflammatory components prevail.

7.3. The proliferative phase (10 and 14 days after wounding) results in regeneration of epidermis, neoangiogenesis and proliferation of fibroblasts with increased collagen synthesis and closure of the skin defect.

7.4. The final remodeling phase takes place over 6 months.

7.5. In my opinion, it is evident that the areas of scarring for samples A and B are about equal to C and D on day 3 because this is the time of lag phase where inflammatory components prevail over the proliferation phase and, therefore, new tissue is not yet made. On day 1, the lag phase is starting and one can value an initial effect of the samples according to the invention. Nevertheless, on day 3 the lag phase is to maximum expression and the inflammation prevails over the samples' effects. Only in the proliferation phase (on day 14), can one estimate the real effect of the samples A and B according to the present invention.

8. Explanation of test results in Attachment 1 – I also understand that the Examiners requested some further explanation of the graph results in Attachment 1, namely the graph relating to "Effective hyaluronate formulations on wound coverage". Indication in the graph of the "wound coverage" is based on a score related to the length of epidermal coverage as a measure of "re-epithelialization". Thus, an increased number for "wound coverage" represents an increased amount of re-epithelialization, which is a positive result. The graph shows that tests D and E according to the present invention exhibited increased wound coverage (namely improved re-epithelialization); whereas, the comparative tests A, B and C showed wound coverage values either about the same as control or actually less than control. In addition, presented below in Table 1 are the quantitative of values of improvement for the tested samples, wherein samples D and E according to the present invention were compared to the other samples, and wherein it is assumed that the value of wound coverage obtained with the control "alginate vehicle" is 100.

Table 1:

| A | B | C | D | E | F |
|---|---|---|---|---|---|
| 100 | 110 | 101 | 140 | 138 | 110 |

From these results it can be seen that samples D and E according to the present invention exhibited an improvement of about 40% in the wound coverage versus all control samples.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated:

MARCH 5, 2009

By _____
Anna Maria Zanellato

# *CURRICULUM VITAE*
## *Anna Zanellato*

I, Anna Zanellato, being duly sworn, depose and say that:

- I am an Italian citizen residing at Bovolenta, Padua, Italy
- I am familiar with the English language.

I further declare that:

- I graduated in Biology at the University of Padua in the academic year 1987
- I am author of 19 scientific publications.

Previous job experience:

- From 1987 to 1990 I worked at the University Department of General Pathology as researcher, where I was involved in a study pertaining to smooth muscles cell cultures; moreover I studied the variations in myosin compositions that occur in situations of vascular pathologies such as Hypertension and Atherosclerosis.

- In the years 1990-2001, I worked at Fidia farmaceutici as senior researcher and my research activity involved: analysis of the action mechanism of various trophic factors of the central nervous system; studies utilising neuronal cultures to select new, pharmacologically active, chemical molecules to prevent different types of neuronal pathologies; other studies concerning the growth and proliferation of bovine, rabbit, human, mesenchymal/articular/fibroblastic cell cultures on biomaterials.

Current job:

- I am working as Scientific Assistant to the Fidia farmaceutici. Patent Department, Italy.